

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 3, line 24 with the following amended paragraph:

Another aspect of the disclosure provides a DNA repair modulator targeting DNA-PKcs activity. One such modulator includes, but is not limited to, a polypeptide such as a single chain antibody variable fragment (scFv). In a particular aspect, the scFv recognizes a 24 ~~25~~ residue linear peptide unique to DNA-PKcs, outside the conserved protein kinase catalytic domain. The scFv sensitizes cells to radiation by altering DSB repair in situ in living cells. Methods for screening for DNA repair modulators and for treating cancer are also provided.

Please replace the paragraph beginning on page 21, line 12 with the following amended paragraph:

The term "nuclear localization signal" or "NLS" includes, but is not limited to, polypeptides or modified polypeptides that facilitate translocation of a substance into the nucleus. Representative NLS include, but are not limited to, Large T (PKKKRKVC) (SEQ. ID NO.:1); MA-NLS1 (GKKKYKLKH) (SEQ. ID NO.:2); MA-NLS2 (KSKKKAQ) (SEQ. ID NO.:3); IN-NLS (KRK and KELKQKQITK) (SEQ. ID NO.:4); Vpr N (NEWTLELLEELKNEAVRHF) (SEQ. ID NO.:5); Vpr C (RHSRIGVTRGRRARNGASRS) (SEQ. ID NO.:6); Tat-NLS (RKKRRQRRR) (SEQ. ID NO.:7); Rev NLS (RQARRNRRRRWR) (SEQ. ID NO.:8); H2B (GKKRSKV) (SEQ. ID NO.:9); v-Jun (KSRKRKL) (SEQ. ID NO.:10); nucleoplasmin (RPAATKKAGQAKKKKLDK) (SEQ. ID NO.:11); NIN2 (RKKRKTEESPLKDKAKKSK) (SEQ. ID NO.:12); or SWI5 (KKYENVVIKRSRKRGRPRK) (SEQ. ID NO.:13). It will be appreciated that the NLS can be selected from those listed in NLSdb ~~available at (http://cubic.bioc.columbia.edu/db/NLSdb/)~~ which is incorporated by reference in its entirety.

Please replace the paragraph beginning on page 39, line 19 with the following amended paragraph:

Surface plasmon resonance measurement were made using a Biacore X instrument (Biacore, Piscataway, N.J.). Interaction between scFv 18-2 and purified DNA-PKcs was measured by amine coupling of scFv to one channel of a Biosensor chip CM-5. The other channel was used as a reference. Analyte, consisting of purified DNA-PKcs diluted in HBS-EP (10 mM HEPES, pH 7.4, 150 mM NaCl, 3 mM EDTA, 0.005% Surfactant P20) was flowed over the chip at 30 μ l/min. Interaction between scFv and peptides was measured by immobilizing the specific peptide, ~~biotin-KKKYIEIRKEAREAANGDSDGPSYM~~ biotin-KKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16), in one channel of a Biosensor chip SA and a non-specific peptide, representing a nearby non-binding sequence, LADSTLSEEMSQFDFSTGVQSYSYS (SEQ. ID NO.:34), in the other channel. Analyte, consisting of scFv 18-2 diluted in HBS-EP, was flowed over the chip as above. For both experiments, regeneration between runs was with HBS-EP supplemented with 4 mM MgCl₂, 100 mM glycine, pH 2.3, and 1 M NaCl. Duplicate measurements were made at 25.degree. C. Data were additionally double referenced and evaluated using the 1:1 interaction with the mass transfer limitation model of the BioEvaluation 3.1 software.

Please replace the paragraph beginning on page 43, line 14 with the following amended paragraph:

The epitope was further delineated using overlapping cDNAs providing full coverage of the 1-2713 fragment. Proteins were expressed using a coupled in vitro transcription-translation system and scFv 18-2 binding was tested by immunoprecipitation with anti-epitope tag antibody. The epitope mapped to fragment spanning residues 1734-2228 (FIG. 1D). This sequence was further subcloned (not shown) and studies with synthetic peptides (FIG. 1F) identified at 24 ~~25~~ residue sequence, 2001-2025, as necessary and sufficient for epitope formation. Surface plasmon resonance showed that binding parameters for interaction between scFv and the peptide were comparable to those for interaction with whole DNA-PKcs (FIG. 1G). The epitope mapping is summarized in FIG. 1H. The epitope is located outside the kinase catalytic domain, within sequences unique to DNA-PKcs and not shared with ATM or ATR.